

Sub E1  
cont.  
D  
cont.

acids, wherein said nucleotide sequence encoding a naturally occurring artemin amino acid sequence consists of not more than 10,000 nucleotides [or a conservatively substituted variant thereof], and wherein said artemin amino acid sequence is at least 65% identical to SEQ ID NO:26 or a fragment thereof, and promotes survival of neurons [of at least 8 contiguous amino acids which nucleotide sequence is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62], and which polynucleotide also comprises a nucleotide sequence encoding a fragment containing an active domain of at least one other growth factor from the TGF- $\beta$  superfamily.

Sub E2

15. (Three times amended) An isolated and purified nucleic acid molecule or fragment thereof consisting of no more than 10,000 nucleotides, wherein the isolated and purified nucleic acid molecule comprises a nucleotide sequence [encoding] that encodes [an] a naturally occurring artemin amino acid sequence that is at least 65% identical to SEQ ID NO:26 or a fragment thereof, and promotes survival of neurons. [or a conservatively substituted variant thereof, which nucleic acid molecule or fragment thereof contains from at least 15 to no more than about 10,000 nucleotides and is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62.]

D2

16. (Twice amended) The isolated and purified nucleic acid molecule of claim 15, wherein the [nucleic acid molecule comprises a nucleotide sequence encoding an] artemin polypeptide [which] promotes survival of trigeminal ganglion neurons, nodose ganglion neurons, superior cervical ganglion neurons, and tyrosine-hydroxylase-expressing dopaminergic ventral midbrain neurons [wherein said nucleic acid molecule specifically hybridizes to a nucleotide sequence encoding mature human artemin as set forth in SEQ ID NO:6, SEQ ID NO:7 or SEQ ID NO:8 or to a nucleotide sequence encoding mature mouse artemin as set forth in SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39, or to the complement of said sequence].

Sub G2

17. (Amended) The isolated and purified nucleic acid molecule [or nucleic acid molecule complementary thereto] of claim [16] 15 comprising a nucleotide sequence encoding an artemin polypeptide as set forth in SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:34, SEQ ID NO:35 or SEQ ID NO:36.

3  
Pnt 18. (Amended) The isolated and purified nucleic acid molecule [or nucleic acid molecule complementary thereto] of claim 17 comprising a nucleotide sequence as set forth in SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39 or SEQ ID NO:44.

Sub E3  
D4  
25. (Twice amended) A recombinant nucleic acid molecule comprising an artemin nucleotide sequence wherein the artemin nucleotide sequence encodes [an] naturally occurring artemin amino acid sequence selected from the group consisting of a pre-pro-artemin polypeptide, a pro-artemin polypeptide, a mature artemin polypeptide, a conservatively substituted variant thereof] and a fragment of said pre-pro-artemin amino acid sequence having at least 8 contiguous amino acids, and wherein the artemin [nucleotide sequence is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62.] amino acid sequence is at least 65% identical to SEQ ID NO:26 and promotes survival of neurons.

Sub E4  
D5  
27. (Twice amended) An isolated and purified nucleic acid molecule comprising a polynucleotide encoding:  
(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;  
(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57;  
(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59; or  
(d) [a conservatively substituted variant of (a), (b) or (c) wherein the polynucleotide encoding said conservatively substituted variant is capable of specifically hybridizing to a nucleic acid sequence selected from the group consisting of SEQ ID NO:24, SEQ ID NO:27, SEQ ID NO:30 and SEQ ID NO:46, or a complement thereof.] a polypeptide that is at least 65% identical to (a), (b) or (c).

D6  
39. (Amended) The [nucleic acid comprising a ] polynucleotide [encoding a pan-growth factor] according to claim 12, wherein the at least one other growth factor from the TGF- $\beta$  superfamily is selected from the group consisting of transforming growth factor- $\beta$ 1 (TGF $\beta$ 1), transforming growth factor- $\beta$ 2 (TGF $\beta$ 2), transforming growth factor- $\beta$ 3 (TGF $\beta$ 3), inhibin  $\beta$  A (INH $\beta$ A), inhibin  $\beta$  B (INH $\beta$ B), the *nodal* gene (NODAL), bone morphogenetic proteins 2 and 4 (BMP2 and BMP4), the *Drosophila decapentaplegic* gene (*dpp*), bone morphogenetic proteins 5-8 (BMP5, BMP6, BMP7 and BMP8), the *Drosophila* 60A gene family (60A), bone morphogenetic protein 3 (BMP3), the *Vgl* gene, growth differentiation factors 1 and 3 (GDF1 and GDF3), dorsalin (*drsln*), inhibin  $\alpha$  (INH $\alpha$ ), the *MIS* gene